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**To: Peter O'Sullivan, Examiner**  
Assistant Commissioner for Patents

**Facsimile: 703-308-4556**  
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**From: Kawai Lau**

**Date: September 18, 2000**

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**Ref: 27510-20010.21 - Serial No.: 09/396,523**



**UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office**

Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

MAR 6 2000

NO. APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
US/341,400	09/09/99	VERMEULIN	N 275102001020

HM12/0302

KATE H MURASHIGE  
MORRISON & FOERSTER  
2000 PENNSYLVANIA AVENUE NW  
SUITE 5500  
WASHINGTON DC 20006-1888

EXAMINER
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HENLEY III, R

ART UNIT	PAPER NUMBER
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1614

5

DATE MAILED: 03/02/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

DOCKETED  
RESPONSE DUE 6/2/2000  
FINAL DATE 9/2/2000

**Office Action Summary**Application No.  
09/341,400Applicant(s)  
Nicolaas Vermeulin et al.Examiner  
Ray HenleyGroup Art Unit  
1614☐ Responsive to communication(s) filed on \_\_\_\_\_☐ This action is **FINAL**.☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle* 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claim**☒ Claim(s) 36-57 is/are pending in the application

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration

☒ Claim(s) 36-55 is/are allowed.☒ Claim(s) 56 and 57 is/are rejected.☐ Claim(s) \_\_\_\_\_ is/are objected to.☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.**Application Papers**☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.☐ The specification is objected to by the Examiner.☐ The oath or declaration is objected to by the Examiner.**Priority under 35 U.S.C. § 119**☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).☐ All ☐ Some\* ☒ None of the CERTIFIED copies of the priority documents have been  
☐ received.☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).**Attachment(s)**☒ Notice of References Cited, PTO-892☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_☐ Interview Summary, PTO-413☒ Notice of Draftsperson's Patent Drawing Review, PTO-948☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Application/Control Number: 09/341,400

Page 2

Art Unit: 1614

### **CLAIMS 36-57 ARE PRESENTED FOR EXAMINATION**

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Applicants' amendment filed July 6, 1999 has been received and entered into the application. Accordingly, claims 1-35 have been canceled and claims 36-57 have been added.

Applicants should note that the references cited on the attached form PTO-892 are those that were cited in the priority documents. No copies have been furnished.

#### ***Claim Rejection - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 56-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are deemed indefinite because none the preceding claims provide antecedent basis for the numeric identification of the compounds.

#### ***Allowable Subject Matter***

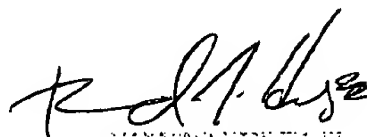
Claims 36-55 are deemed to be in condition for allowance because none of the prior art teaches the present method of synthesis of a polyamine analogue or the analogues produced thereby.

Application/Control Number: 09/341,400

Page 3

Art Unit: 1614

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Henley whose telephone number is (703) 308-4652.



RAY HENLEY, JR.  
PATENT EXAMINER  
ART UNIT 1614

Henley; rjh  
February 28, 2000

**Notice of References Cited**Application No.  
09/341,400Applicant(s)  
Nicolaas Vermeulin et al.Examiner  
Ray HenleyGroup Art Unit  
1614

Page 1 of 2

**U.S. PATENT DOCUMENTS**

* <input type="checkbox"/>	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS
<input type="checkbox"/> A					
<input type="checkbox"/> B					
<input type="checkbox"/> C					
<input type="checkbox"/> D					
<input type="checkbox"/> E					
<input type="checkbox"/> F					
<input type="checkbox"/> G					
<input type="checkbox"/> H					
<input type="checkbox"/> I					
<input type="checkbox"/> J					
<input type="checkbox"/> K					
<input type="checkbox"/> L					
<input type="checkbox"/> M					

**FOREIGN PATENT DOCUMENTS**

* <input type="checkbox"/>	DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUBCLASS
<input checked="" type="checkbox"/> N	WO 95/21612	8/95	PCT	NPS Pharma Inc.	---	---
<input checked="" type="checkbox"/> D	WO 85/02769	7/85	PCT	Kovacs Adam	---	---
<input type="checkbox"/> P						
<input type="checkbox"/> Q						
<input type="checkbox"/> R						
<input type="checkbox"/> S						
<input type="checkbox"/> T						

**NON-PATENT DOCUMENTS**

* <input type="checkbox"/>	DOCUMENT (Including Author, Title, Source, and Pertinent Pages)	DATE
<input checked="" type="checkbox"/> U	Karahalos et al., Eur. J. Biochem. 251(3), 998-1004.	1998
<input checked="" type="checkbox"/> V	Veznick et al., Helvetica Chimica Acta., vol. 74, pp 654-661	1991
<input checked="" type="checkbox"/> W	Carrington et al., Pharm. Sci. 2(1), 25-27.	1996
<input checked="" type="checkbox"/> X	Qaraw et al., Pharm. Sci. 3(5/6) 235-239.	1997

**Notice of References Cited**Application No.  
09/341,400Applicant(s)  
Nicolaas Vermeulen et al.Examiner  
Ray HenleyGroup Art Unit  
1614

Page 2 of 2

**U.S. PATENT DOCUMENTS**

* A	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS
B					
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J					
K					
L					
M					

**FOREIGN PATENT DOCUMENTS**

* N	DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUBCLASS
O						
P						
Q						
R						
S						
T						

**NON-PATENT DOCUMENTS**


* U	DOCUMENT (Including Author, Title, Source, and Pertinent Pages)	DATE
X	Chao et al., Mol. Pharmacol. 51(5), 861-871.	1997
X	Green et al., Brain Research 717/1-2, 135-146.	1996
W		
X		

A copy of this reference is not being furnished with this Office action.  
(See Manual of Patent Examining Procedure, Section 707.05(a).)

PATENT  
Docket No. 275102001020

**CERTIFICATE OF HAND DELIVERY**

I hereby certify that this correspondence is being hand filed with the United States Patent and Trademark Office in Washington, D.C. on June  
/ , 2000.

  
Sherri N. Shipa

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In the application of:

Nicolaas M.J. VERMEULIN et al.

Serial No.: 09/341,400

Filing Date: 6 July 1999

For: NOVEL POLYAMINE ANALOGUES  
AS THERAPEUTIC AND DIAGNOSTIC  
AGENTS

Examiner: R. Henley III

Group Art Unit: 1614

**REPLY WITH AMENDMENT UNDER 37 C.F.R. § 1.111**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

This is in response to an Office Action mailed March 2, 2000, time for response to which was set to expire June 2, 2000. Given this timely response, no Petition for Extension of Time is believed required.

Claims 36-57 are pending with claims 56 and 57 rejected. Claims 36-55 have been indicated as allowable. Reconsideration in view of the following amendments and remarks is respectfully requested.

dc-210249



**AMENDMENT**

Please amend the claims as follows:

56. (amended) A library according to claim 43 wherein said library comprises one or more polyamine analogues [is] selected from the group consisting of compounds designated in Figure 2 as 3, 4, 5, 6, 13, 14, 29, 40, 43, 44, 45, 57, 58, 56, 66, 67, 72, 76, 84, 88, 89, 95 and 96.

57. (amended) A [composition] library according to claim 56, wherein said library comprises one or more polyamine analogues [is] selected from the group consisting of compounds designated in Figure 2 as 4, 5, 6, 43, 65, 66, 84, 89, 95 or 96.

Please add the following new claims:

58. A library of polyamine compounds comprising one or more polyamine analogues selected from the group consisting of compounds designated in Figure 2 as 3, 4, 5, 6, 13, 14, 29, 40, 43, 44, 45, 57, 58, 56, 66, 67, 72, 76, 84, 88, 89, 95 and 96.

59. The library according to claim 58, wherein said library comprises one or more polyamine analogues selected from the group consisting of compounds designated in Figure 2 as 4, 5, 6, 43, 65, 66, 84, 89, 95 or 96.

**REMARKS**

The above amendments to claims 56 and 57 merely improve clarity of the relationship of the recited compounds to the claimed libraries; reference the numerical identifiers to Figure 2; and clarify the relationship between the two claims. New claims 58 and 59 are directed to the same subject matter of claims 56 and 57 except without being in a "product by process" format.

No new matter has been introduced and the intended scope of claims 56 and 57 have not been altered. Entry of the amendment is respectfully requested.

***Rejection under 35 USC § 112, Second Paragraph***

Pending claims 56 and 57 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite for not providing antecedent basis for the numeric identification of the compounds.

Claims 56 and 57 have been amended to more clearly relate the claimed libraries to the recited compounds. Specifically, the claimed libraries may comprised one or more of the recited compounds.

The representation of the recited compounds by numerical identifiers with reference to Figure 2 of the instant application introduces no indefiniteness since the nature of the compounds is completely clear when the claims are read in light of the specification and drawings.

Applicants respectfully submit that the rejection has been obviated and request its withdrawal.

**Conclusion**

In light of the above amendments and remarks, Applicants respectfully submit that the claims are in condition for immediate allowance, and passage of the application to issue is urged. The Examiner is welcome to contact the undersigned if he determines that further discussions would prove useful.

In the unlikely event that the Transmittal Letter is separated from this document and/or the Patent Office determines that a further extension and/or other relief or fees are required, Applicants hereby petition for any required relief including extensions of time, payment of claim fees, and the like, and authorize the Assistant Commissioner to charge the cost of such petitions

and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing 275102001020. However, the Assistant Commissioner is **not** authorized to charge the cost of the Issue Fee to the Deposit Account.

Dated: June 1, 2000

Respectfully submitted,

By: 

Kawai Lau, Ph.D.  
Registration No. 44,461

Morrison & Foerster LLP  
2000 Pennsylvania Avenue, N.W.  
Washington, D.C. 20006-1888  
Telephone: (202) 887-6939  
Facsimile: (202) 887-0763



JOHN F. MURPHY  
DIRECTOR, PLANNING  
2000 PLANNING PARTNERS ASSOCIATES, INC.  
1115 BELL  
WASHINGTON, DC 20004-1005

TITLE OF INVENTION: METHOD FOR VIBRATION SUPPLEMENTATION OF HIGH-SPEED CUT AND FINISHING OPERATION

**THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT.  
PROSECUTION ON THE MERITS IS CLOSED.**

**THE ISSUE FEE MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED.**

Review the SMALL ENTITY status shown above.  
If the SMALL ENTITY is shown as YES, verify your  
current SMALL ENTITY status:

- A. If the status is changed, pay twice the amount of the **FEE DUE** shown above and notify the Patent and Trademark Office of the change in status, or
- B. If the status is the same, pay the **FEE DUE** shown above.

If the SMALL ENTITY is shown as NO:

**DOCKETED**

ISSUE FEE DUE 9/21/00  
J. Drudge 9/21 LD 12/21/00

- A. Pay FEE DUE shown above, or**

- B. File verified statement of Small Entity Status before, or with, payment of 1/2 the FEE DUE shown above.**

**Part B-Issue Fee Transmittal** should be completed and returned to the Patent and Trademark Office (PTO) with your **ISSUE FEE**. Even if the **ISSUE FEE** has already been paid by charge to deposit account, **Part B Issue Fee Transmittal** should be completed and returned. If you are charging the **ISSUE FEE** to your deposit account, section "4b" of **Part B-Issue Fee Transmittal** should be completed and an extra copy of the form should be submitted.

**1. All communications regarding this application must give application number and batch number.**

Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER:** Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

## YOUR COPY

TOL-85 (REV. 10-96) Approved for use through 06/30/99. (0651-0033)

\*U.S. GPO: 1989-454-457/24801

09/18/00 MON 17:33 [TX/RX NO 6820] 012

## PART B—ISSUE FEE TRANSMITTAL

Complete and mail this form, together with applicable fees, to: **Box ISSUE FEE**  
**Assistant Commissioner for Patents**  
**Washington, D.C. 20231**

**MAILING INSTRUCTIONS:** This form should be used for transmitting the ISSUE FEE. Blocks 1 through 4 should be completed where appropriate. All further correspondence including the Issue Fee Receipt, the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Legibly mark-up with any corrections or use Block 1)

KATE H MURASHIGE  
 MORRISON & FORDERSTER  
 2000 PENNSYLVANIA AVENUE NW  
 SUITE 5500  
 WASHINGTON DC 20006-1888

HM22/0621

Note: The certificate of mailing below can only be used for domestic mailings of the Issue Fee Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing.

## Certificate of Mailing

I hereby certify that this Issue Fee Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Box Issue Fee address above on the date indicated below.

(Depositor's name)

(Signature)

(Date)

APPLICATION NO.	FILING DATE	TOTAL CLAIMS	EXAMINER AND GROUP ART UNIT	DATE MAILED
09/341,400	09/03/99	024	HENLEY III, R	1614 06/21/00
First Named Applicant	VERMEULIN,	35 USC 154(b) term ext. =	0 Days.	

**TITLE OF INVENTION** NOVEL POLYAMINE ANALOGUES AS THERAPEUTIC AND DIAGNOSTIC AGENTS

ATTYS DOCKET NO.	CLASS-SUBCLASS	BATCH NO.	APPLN. TYPE	SMALL ENTITY	FEE DUE	DATE DUE
1 275102001020	554-084.000	038	UTILITY	YES	\$695.00	09/21/00

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363). Use of PTO form(s) and Customer Number are recommended, but not required.

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47) attached.

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 \_\_\_\_\_  
 2 \_\_\_\_\_  
 3 \_\_\_\_\_

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)  
**PLEASE NOTE:** Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the PTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY & STATE OR COUNTRY)

Please check the appropriate assignee category indicated below (will not be printed on the patent)

☐ individual ☐ corporation or other private group entity ☐ government

4a. The following fees are enclosed (make check payable to Commissioner of Patents and Trademarks):

☐ Issue Fee  
☐ Advance Order - # of Copies \_\_\_\_\_

4b. The following fees or deficiency in these fees should be charged to:

DEPOSIT ACCOUNT NUMBER \_\_\_\_\_  
 (ENCLOSE AN EXTRA COPY OF THIS FORM)

☐ Issue Fee  
☐ Advance Order - # of Copies \_\_\_\_\_

The COMMISSIONER OF PATENTS AND TRADEMARKS IS requested to apply the Issue Fee to the application identified above.

(Authorized Signature)

(Date)

NOTE: This Issue Fee will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the Patent and Trademark Office.

**Burden Hour Statement:** This form is estimated to take 0.2 hours to complete. Time will vary depending on the needs of the individual case. Any comments on the amount of time required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND FEES AND THIS FORM TO: Box Issue Fee, Assistant Commissioner for Patents, Washington D.C. 20231

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

TRANSMIT THIS FORM WITH FEE

**Notice of Allowability**Application No.  
09/341,400Applicant(s)  
Nicolaas M.J. Vermeulin, et al.Examiner  
Ray HenleyGroup Art Unit  
1614

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course.

☒ This communication is responsive to the papers filed 2/8/2000 and 6/1/2000

☒ The allowed claim(s) is/are 36-59

☐ The drawings filed on \_\_\_\_\_ are acceptable.

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE THREE MONTHS FROM THE "DATE MAILED" of this Office action. Failure to timely comply will result in ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

☐ Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.

☒ Applicant MUST submit NEW FORMAL DRAWINGS

☐ because the originally filed drawings were declared by applicant to be informal.

☒ including changes required by the Notice of Draftsperson's Patent Drawing Review, PTO-948, attached hereto or to Paper No. 6.

☐ including changes required by the proposed drawing correction filed on \_\_\_\_\_, which has been approved by the examiner.

☐ including changes required by the attached Examiner's Amendment/Comment.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the reverse side of the drawings. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

☐ Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any response to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE/SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

**Attachment(s)**

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 7

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☐ Interview Summary, PTO-413

☒ Examiner's Amendment/Comment

☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material

☐ Examiner's Statement of Reasons for Allowance

Application/Control Number: 09/341,400

Page 2

Art Unit: 1614

# **EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

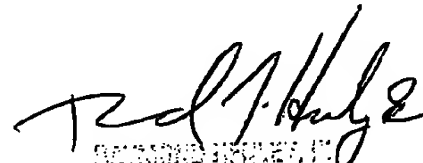
The application has been amended as follows:

## **IN THE SPECIFICATION:**

At page 1, first line after the title, the following has been inserted:

---This application claims priority under 35 USC 119(e) over provisional application No.s 60/052,586, filed July 15, 1997, 60/065,728, filed November 14, 1997 and 60/085,538, filed May 15, 1998 and this application is a 371 of PCT/US98/14896, filed July 15, 1998.---

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Henley whose telephone number is (703) 308-4652.

  
 EXAMINER  
 PRIMARY EXAMINER  
 GROUP 400

Henley, rjh  
 June 10, 2000

**Patent****Atty Docket No.: 27510-20010.20****Allowed Claims**

36. A method for the synthesis of a polyamine analogue by chain extension comprising

1) attaching a cleavable linker to activate a soluble or insoluble support followed sequentially by

attaching, to said linker, one or more extender synthons comprising free amino and protected aldehyde moieties, and

attaching, to the last extender synthon, a chain terminator so that a desired polyamine containing chain is present; and

2) cleaving the polyamine chain from the support,  
wherein said attached synthons may be additionally reduced by reductive amidation.

37. The method of claim 36 wherein said attaching step comprises

a) attaching to the soluble or insoluble support a cleavable linker containing a first amide bond with an activated leaving moiety;

b) attaching via the first amide bond a first extender synthon containing a free amino moiety and a protected aldehyde moiety;

c) deprotecting the protected aldehyde moiety;

d) optionally attaching, via the deprotected aldehyde moiety, one or more additional extender synthons by repeating steps b) and c), where step b) is reductive amination; and

e) reacting the deprotected aldehyde moiety with an amine under reductive amination conditions and attaching an aldehyde containing chain terminator;

wherein reductive amination of a secondary amine with an aldehyde in the extending chain may optionally occur after each attaching step b).

sd-9938



38. The method of claim 36 or 37 wherein the cleavable linker yields polyamine chains with an alcohol group, amide or substituted amides upon cleavage.

39. The method of claim 36 or 37 wherein the support is selected from the group consisting of MeO-polyethylene glycol-OH, 3,4-dihydro-2H-pyran-2-yl-methoxymethyl polystyrene, polystyrene resins, chip-based systems, multi-pin systems and hydroxyl group containing microwells;

the extender synthon is a free amino and protected aldehyde moieties containing form of a compound selected from the group consisting of chiral amino acids and amino acid precursors, reactive moieties that bind polyamine binding molecules, aliphatic structures, aromatic structures, heterocyclic structures, carbohydrates, nucleosides, and known drug agents, each of which contains a free amino moiety and a protected aldehyde moiety; and

the chain terminator is selected from the group consisting of acrolein, unsaturated alkene aldehydes, straight chain alkyl aldehydes, and branched chain alkyl aldehydes.

40. The method of claim 39 wherein the extender synthon is a free amino and protected aldehyde moieties containing form of a compound selected from the group consisting of

Alinol	2-amino-2-methyl-1-propanol
L-methioninol	D-glucosamine
R,S-2-amino-1-butanol	4-aminobutanol
3-amino-1-propanol	trans-2-aminocyclohexanol
5-aminopentanol	(S)-(+)-2-amino-3-cyclohexyl-1-propanol
R,S-2-amino-2-phenylethanol	DL-2-amino-1-hexanol
6-amino-1-hexanol	1-(1S,2S)(+)-2-amino-3-methoxy-1-phenyl-1-propanol
2-amino-3-methyl-1-pentanol	2-amino-4-methyl-1-pentanol
2-(2-amino-4-nitroanilino)ethanol	D,L-2-amino-1-pentanol
2-aminophenethyl alcohol	2-amino-1-phenylethanol
2-amino-3-methyl-1-pentanol	(R)-(+)-2-amino-3-phenyl-1-propanol
(S)-(-)-2-amino-3-phenyl-1-propanol	2-(3-aminophenylsulfonyl)ethanol
D,L-1-amino-2-propanol	D,L-2-amino-1-propanol
3-amino-1-propanol	D-galactosamine and
D-mannosamine.	

41. The method of claim 36 or 37 wherein the steps are conducted in parallel using more than one extender synthon and more than one chain terminator.

42. A library of polyamine derivatives produced by the method of claim 41.

43. The library of claim 42, wherein said derivatives have the formula



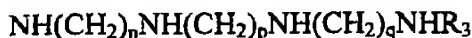
wherein

$R_1$  is H, or is a head group selected from the group consisting of a straight or branched  $C_{1-10}$  aliphatic, alicyclic, single or multiring aromatic, single or multiring aryl substituted aliphatic, aliphatic-substituted single or multiring aromatic, a single or multiring heterocyclic, a single or multiring heterocyclic-substituted aliphatic and an aliphatic-substituted aromatic;

$R_2$  is a polyamine; and

X is CO, NHCO, NHCS, or SO<sub>2</sub>

44. A library according to claim 43 wherein  $R_2$  has the formula



wherein

- (a)  $n$ ,  $p$  and  $q$  vary independently and  $n=p=q=1$  to  $12$ ;
- (b)  $R_3$  is H;  $C_{1-10}$  alkyl;  $C_{1-10}$  alkenyl;  $C_{1-10}$  alkynyl; alicyclic; aryl; aryl-substituted alkyl, alkenyl or alkynyl; alkyl-, alkenyl-, or alkynyl-substituted aryl; guanidino; heterocyclic; heterocyclic-substituted alkyl, alkenyl or alkynyl; and alkyl-, alkenyl-, or alkynyl-substituted heterocyclic.

45. A library according to claim 43, wherein the derivatives further comprise, linked between  $X$  and  $R_2$ , a linker  $L$  and an additional group  $y$ , such that the derivatives have the formula:



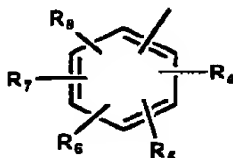
wherein,

$L$  is a  $C_{1-10}$  alkyl,  $C_{1-10}$  alkenyl,  $C_{1-10}$  alkynyl, alicyclic, or heterocyclic;

$X$  is  $\text{CO}$ ,  $\text{SO}_2$ ,  $\text{NHCO}$  or  $\text{NHCS}$ ; and

$Y$  is  $\text{CONH}$ ,  $\text{SO}_2\text{NH}$ ,  $\text{NHCO}$ ,  $\text{NHCONH}$ ,  $\text{NHCSNH}$ ,  $\text{NHSO}_2$ ,  $\text{SO}_2$ ,  $\text{O}$ , or  $\text{S}$ .

46. A library according to claim 43 where  $R_1$  has the formula:

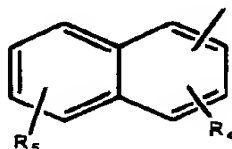


wherein

$R_4$ ,  $R_5$ ,  $R_6$ ,  $R_7$  and  $R_8$  are, independently, H, OH, halogen,  $\text{NO}_2$ ,  $\text{NH}_2$ ,  $\text{NH}(\text{CH})_n\text{CH}_3$ ,  $\text{N}((\text{CH})_n\text{CH}_3)_2$ , CN,  $(\text{CH})_n\text{CH}_3$ ,  $\text{O}(\text{CH})_n\text{CH}_3$ ,  $\text{S}(\text{CH}_2)_n\text{CH}_3$ ,  $\text{NCO}(\text{CH}_2)_n\text{CH}_3$ ,  $\text{O}(\text{CF}_2)_n\text{CF}_3$ , or  $\text{CO-O}(\text{CH})_n\text{CH}_3$  where  $n=0$  to  $10$ ;

sd-9938

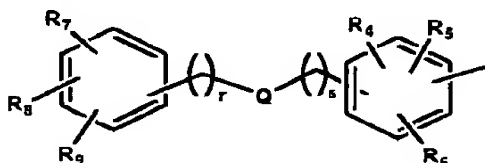
47. A library according to claim 43 where  $R_1$  has the formula:



wherein

$R_4$  and  $R_5$  are, independently, H, OH, halogen,  $\text{NO}_2$ ,  $\text{NH}_2$ ,  $\text{NH}(\text{CH})_n\text{CH}_3$ ,  $\text{N}((\text{CH})_n\text{CH}_3)_2$ , CN,  $(\text{CH})_n\text{CH}_3$ ,  $\text{O}(\text{CH})_n\text{CH}_3$ ,  $\text{S}(\text{CH}_2)_n\text{CH}_3$ ,  $\text{NCO}(\text{CH}_2)_n\text{CH}_3$ ,  $\text{O}(\text{CF}_2)_n\text{CF}_3$ , or  $\text{CO-O}(\text{CH})_n\text{CH}_3$ , where  $n=0$  to 10;

48. A library according to claim 43 wherein  $R_1$  has the formula:



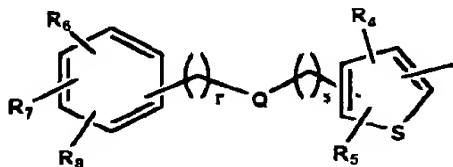
wherein

$r$  and  $s$  vary independently and  $r=s=0$  to 6;

$R_4$ ,  $R_5$ ,  $R_6$ ,  $R_7$ ,  $R_8$  and  $R_9$  are, independently, H, OH, halogen,  $\text{NO}_2$ ,  $\text{NH}_2$ ,  $\text{NH}(\text{CH})_n\text{CH}_3$ ,  $\text{N}((\text{CH})_n\text{CH}_3)_2$ , CN,  $(\text{CH})_n\text{CH}_3$ ,  $\text{O}(\text{CH})_n\text{CH}_3$ ,  $\text{S}(\text{CH}_2)_n\text{CH}_3$ ,  $\text{NCO}(\text{CH}_2)_n\text{CH}_3$ ,  $\text{O}(\text{CF}_2)_n\text{CF}_3$ , or  $\text{CO-O}(\text{CH})_n\text{CH}_3$  where  $n=0$  to 10; and

$Q$  is CONH,  $\text{SO}_2\text{NH}$ ,  $\text{NHCO}$ ,  $\text{NHCONH}$ ,  $\text{NHCSNH}$ ,  $\text{NH}\text{SO}_2$ ,  $\text{SO}_2$ , O, or S.

49. A library according to claim 43 wherein  $R_1$  has the formula:



wherein  $r$  and  $s$  vary independently and are 0 to 6;

sd-9938

$R_4$ ,  $R_5$ ,  $R_6$  and  $R_7$  are, independently, H, OH,  $\text{NO}_2$ ,  $\text{NH}_2$ ,  $\text{NH}(\text{CH})_n\text{CH}_3$ ,  $\text{N}((\text{CH})_n\text{CH}_3)_2$ , CN,  $(\text{CH})_n\text{CH}_3$ ,  $\text{O}(\text{CH})_n\text{CH}_3$ ,  $\text{S}(\text{CH}_2)_n\text{CH}_3$ ,  $\text{NCO}(\text{CH}_2)_n\text{CH}_3$ ,  $\text{O}(\text{CF}_2)_n\text{CF}_3$ , or  $\text{CO-O}(\text{CH})_n\text{CH}_3$  where  $n=0$  to 10; and

Q is CONH,  $\text{SO}_2\text{NH}$ , NHCO, NHCONH, NHCSNH,  $\text{NHSO}_2$ ,  $\text{SO}_2$ , O, or S.

50. A library according to claim 43, wherein  $R_1$  is selected from the group consisting of naphthalene, phenanthrene, anthracene, pyrene, dibenzofuran, acridine, 2,1,3-benzothiadiazole, quinoline, isoquinoline, benzofuran, indole, carbazole, fluorene, 1,3-benzodiazine, phenazine, phenoxazine, phenothiazine, adamantane, camphor, piperidine, alkylpiperazine, morpholine, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, thiophene, furan, pyrrole, alkyl-1,2-diazole, alkylimidazole, alkyl-1H-1,2,3-triazol, alkyl-1H-1,2,3,4-tetrazole, thiazole, oxazole, 1,3,4-thiadiazole, pyridinyl, pyrimidine, 1,2-diazine, 1,4-diazine and 1,3,5-triazine, 4-dimethylaminoazobenzene, 3-phenyl-5-methylisooxazole, 3-(2-chlorophenyl)-5-methylisooxazole, 2-(4-chlorophenyl)-6-methyl-7-chloroquinoline, 6-chloroimidazo[2,1- $\beta$ ]thiazole,  $\alpha$ -methylcinnamic acid, and 2-[1,2-dihydro-2H-1,4-benzodioxepinyl]thiazole.

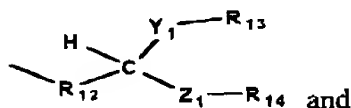
51. A library according to claim 43 wherein  $R_1$  is a D- or L-amino acid.

52. A library according to claim 43 where  $R_1$  has the formula selected from the group consisting of

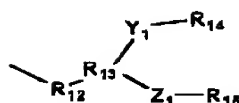
(A)  $R_{12}-R_{13}-Y_1-R_{14}$

(B)  $R_{12}Y_1R_{13}Z_1R_{14}$

(C)



(D)



wherein

$R_{12}$  and  $R_{13}$ , independently, are H, naphthalene, phenanthrene, anthracene, pyrene, dibenzofuran, acridine, 2,1,3-benzothiodiazole, quinoline, isoquinoline, benzofuran, indole, carbazole, fluorene, 1,3-benzodiazine, phenazine, phenoxazine, phenothiazine, adamantane, camphor, piperidine, alkylpiperazine, morpholine, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, thiophene, furan, pyrrole, alkyl-1,2-diazole, alkylimidazole, alkyl-1H-1,2,3-triazol, alkyl-1H-1,2,3,4-tetrazole, thiazole, oxazole, 1,3,4-thiadiazole, pyridinyl, pyrimidine, 1,2-diazine, 1,4-diazine and 1,3,5-triazine, 4-dimethylaminoazobenzene, 3-phenyl-5-methylisooxazole, 3-(2-chlorophenyl)-5-methylisooxazole, 2-(4-chlorophenyl)-6-methyl-7-chloroquinoline, 6-chloroimidazo[2,1- $\beta$ ]thiazole,  $\alpha$ -methylcinnamic acid, or 2-[1,2-dihydro-2H-1,4-benzodioxepinyl]thiazole;

and further,

wherein a ring of  $R_{12}$ ,  $R_{13}$  or both in formulas (A), (B) and (D), is optionally substituted with one or more of OH, halogen,  $\text{NO}_2$ ,  $\text{NH}_2$ ,  $\text{NH}(\text{CH})_n\text{CH}_3$ ,  $\text{N}((\text{CH})_n\text{CH}_3)_2$ , CN,  $(\text{CH})_n\text{CH}_3$ ,  $\text{O}(\text{CH})_n\text{CH}_3$ ,  $\text{S}(\text{CH}_2)_n\text{CH}_3$ ,  $\text{NCO}(\text{CH}_2)_n\text{CH}_3$ ,  $\text{O}(\text{CF}_2)_n\text{CF}_3$ , or  $\text{COO}(\text{CH})_n\text{CH}_3$ , where  $n=0$  to 10;

$R_{14}$  and  $R_{15}$ , and, in formula (C),  $R_{13}$ , independently, are  $(\text{CH}_2)_n$ ,  $(\text{CH}_2)_n\text{CH}=\text{CH}$ ,  $(\text{CH}_2)_n(\text{CH}=\text{CH})_m\text{CO}$ , or  $(\text{CH}_2)_n\text{CO}$  where  $n=0$  to 5 and  $m=1$  to 3;

$Y_1$  and  $Z_1$ , independently, are CONH,  $\text{SO}_2\text{NH}$ , NHCO, NHCONH, NHCSNH,  $\text{NHSO}_2$ ,  $\text{NHSO}_2$ ,  $\text{SO}_2\text{-NHSO}_2$ ,  $\text{SO}_2$ , O, S, COO

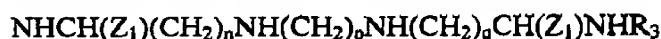
or

when  $R_1$  is of formula (A) or (B),  $Y_1$  represents a bond between a C or N atom of  $R_{12}$  and a C or N atom of  $R_{13}$  and  $Z_1$  represents a bond between a C or N atom of  $R_{13}$  and a C or N atom of  $R_{14}$ ; or

when  $R_1$  is of formula (C) or  $Y_1$  represents a bond between the C and a C or N atom of  $R_{13}$  and  $Z_1$  represents a bond between the C and a C or N atom of  $R_{14}$ ; or

when  $R_1$  is of formula (D)  $Y_1$  represents a bond between a C or N atom of  $R_{12}$  and a C or N atom of  $R_{14}$  and  $Z_1$  represents a bond between a C or N atom of  $R_{13}$  and a C or N atom of  $R_{15}$ .

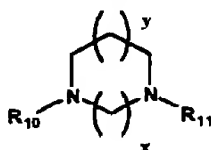
53. A library according to claim 43 wherein  $R_2$  has the formula



and wherein

- (a)  $n$ ,  $p$  and  $q$  vary independently and  $n=p=q=1$  to  $12$ ;
- (b)  $R_3$  is H;  $\text{C}_{1-10}$  alkyl;  $\text{C}_{1-10}$  alkenyl;  $\text{C}_{1-10}$  alkynyl; alicyclic; aryl; aryl-substituted alkyl, alkenyl or alkynyl; alkyl-, alkenyl-, or alkynyl-substituted aryl; guanidino or heterocyclic; and
- (c)  $Z_1$  is  $\text{CH}_3$ ,  $\text{CH}_2\text{CH}_3$  or cyclopropyl.

54. A library according to claim 43 wherein  $R_2$  has the formula:



and wherein

$x=1$  to  $4$ ;  $y=1$  to  $3$ ,

$R_{10}$  and  $R_{11}$  are, independently, H,  $(\text{CH}_2)_n\text{NHR}_{12}$  or  $(\text{CH}_2)_k\text{NH}(\text{CH}_2)_l\text{NHR}_{12}$

where  $n=k=l=1$  to  $10$ , and  $R_{12}$  is H or  $\text{C}(\text{N}=\text{H})\text{NH}_2$

55. A library according to claim 43 wherein  $R_2$  is selected from the group consisting of  $\text{N}^1$ -acetylspermine,  $\text{N}^1$ -acetylspermidine,  $\text{N}^8$ -acetylspermidine,  $\text{N}^1$ -guanidospermine, cadaverine, aminopropylcadaverine, homospermidine, caldine (horspermidine), 7-hydroxyspermidine, thermine (norspermine), thermospermine, canavamine, aminopropylhomospermidine, N, N'-bis(3-aminopropyl)cadaverine,

sd-9938

aminopentyl norspermidine, N<sup>4</sup>-aminopropyl norspermidine, N<sup>4</sup>-aminopropyl spermidine, caldopentamine, homocaldopentamine, N<sup>4</sup>-bis(aminopropyl) norspermidine, thermopentamine, N<sup>4</sup>-bis(aminopropyl) spermidine, caldohexamine, homothermo-hexamine, homocaldohexamine, N-(3-aminopropyl)-1,3-propanediamine, N,N'-bis(3-aminopropyl) ethylenediamine, N,N'-bis(3-aminopropyl)-1,4-piperazine, N,N'-bis(3-aminopropyl)-1,3-piperazine, N,N'-bis(3-aminopropyl)-1,3-propanediamine, N,N'-bis(2-aminoethyl)-1,3-propanediamine, tris(3-aminopropyl)amine, and tris(aminoethyl)amine

56. A library according to claim 43 wherein said library comprises one or more polyamine analogues selected from the group consisting of compounds designated in Figure 2 as 3, 4, 5, 6, 13, 14, 29, 40, 43, 44, 45, 57, 58, 56, 66, 67, 72, 76, 84, 88, 89, 95 and 96.

57. A library according to claim 56, wherein said library comprises one or more polyamine analogues selected from the group consisting of compounds designated in Figure 2 as 4, 5, 6, 43, 65, 66, 84, 89, 95 or 96.

58. A library of polyamine compounds comprising one or more polyamine analogues selected from the group consisting of compounds designated in Figure 2 as 3, 4, 5, 6, 13, 14, 29, 40, 43, 44, 45, 57, 58, 56, 66, 67, 72, 76, 84, 88, 89, 95 and 96.

59. The library according to claim 58, wherein said library comprises one or more polyamine analogues selected from the group consisting of compounds designated in Figure 2 as 4, 5, 6, 43, 65, 66, 84, 89, 95 or 96.

sd-9938